

DiPiro's Pharmacotherapy Handbook, 13th Edition >

Chapter 28: Pancreatitis

INTRODUCTION

- *Acute pancreatitis* (AP) is pancreatic inflammation marked by upper abdominal pain and elevated enzymes.
- *Chronic pancreatitis* (CP) is a progressive condition with persistent inflammation that ultimately impairs exocrine and endocrine function.

ACUTE PANCREATITIS

CLINICAL PRESENTATION

- Clinical presentation depends on the severity of inflammation and whether injury is limited to the pancreas or extends to local or systemic complications.
- Symptoms range from mild abdominal discomfort to severe pain, shock, or respiratory distress. Abdominal pain occurs in 95% of patients, typically epigastric and radiating to the upper quadrants or back. Onset is usually sudden, with “knife-like” or “boring” intensity that peaks within 30 minutes and may last hours to days. Nausea and vomiting occur in about 85% of cases and usually follow the pain.
- Physical findings include marked epigastric tenderness, sometimes with rebound or guarding in severe disease. The abdomen may be distended and tympanic, with decreased or absent bowel sounds.
- Vital signs can be normal, but hypotension, tachycardia, and low-grade fever are common with extensive inflammation or necrosis. Dyspnea and tachypnea indicate respiratory involvement.
- Jaundice or altered mental status may appear, and signs of alcoholic liver disease may accompany alcoholic pancreatitis.
- Many medications have been implicated ([Table 28-1](#)), but drug-induced AP is rare and difficult to confirm because rechallenge is not feasible.



TABLE 28-1

Medications Associated with Acute Pancreatitis

Well-Supported Association	Probable Association	Possible Association	
5-Aminosalicylic acid Asparaginase Azathioprine Bortezomib Carbamazepine Cimetidine Corticosteroids Cisplatin Cytarabine Didanosine Enalapril Erythromycin Estrogens Furosemide Lamivudine Mercaptopurine Mesalamine Octreotide Olsalazine Opioids Pentamidine Pentavalent antimonials Sulfasalazine Sulfamethoxazole and trimethoprim Tamoxifen Tetracyclines Valproic acid/salts	Acetaminophen Hydrochlorothiazide Itraconazole Ifosfamide Interferon α 2b Maprotiline Methyldopa Oxaliplatin	Aldesleukin Amiodarone Atorvastatin Calcium Ceftriaxone Capecitabine Carboplatin Celecoxib Clozapine Cholestyramine Ciprofloxacin Clarithromycin Clonidine Cyclosporine Danazol Diazoxide Etanercept Ethacrynic acid Exenatide Famciclovir Glyburide Gold salts Granisetron Ibuprofen Imatinib	Indinavir Indomethacin Infliximab Ketoprofen Ketorolac Lipid emulsion Liraglutide Lisinopril Mefenamic acid Metformin Metolazone Metronidazole Mirtazapine Nitrofurantoin Omeprazole Ondansetron Paclitaxel Pravastatin Propofol Propoxyphene Rifampin Sertraline Simvastatin Sitagliptin Sorafenib Sulindac Zalcitabine

DIAGNOSIS

- Diagnosis of AP requires two of the following: (1) upper quadrant abdominal pain, (2) serum lipase or amylase at least three times the upper limit of normal, and (3) characteristic imaging findings.
- All patients should undergo right upper quadrant transabdominal ultrasound to detect biliary dilation or gallstones. Contrast-enhanced computed tomography (CECT) is used when clinical and laboratory data are insufficient, while magnetic resonance imaging (MRI) helps assess severity, identify bile duct abnormalities not seen on CECT, or substitute when CECT is contraindicated.
- AP may present with leukocytosis, hyperglycemia, and hypoalbuminemia. Transaminases, alkaline phosphatase, and bilirubin are often elevated in gallstone-related disease or underlying liver disorders. Marked hypocalcemia suggests severe necrosis and poor prognosis.
- Serum amylase usually rises 4–8 hours after symptom onset, peaks at 24 hours, and returns to normal over the next 3–5 days. Concentrations greater than three times the upper limit of normal are highly suggestive of AP.
- Serum lipase is more pancreas-specific, rises in parallel, and stays elevated longer.

- Hematocrit may be normal, but hemoconcentration can occur; hematocrit >47% predicts severe AP, whereas <44% suggests milder disease.
- Elevated or rising blood urea nitrogen (BUN; >20 mg/dL [7.1 mmol/L urea]) within 24 hours correlates with higher mortality.
- The total serum **calcium** is usually normal early, but significant hypocalcemia—beyond what hypoalbuminemia explains—indicates severe necrosis.
- C-reactive protein >190 mg/dL at 48 hours also predicts severe AP.

TREATMENT (FIG. 28-1)

- **Goals of Treatment:** Relieve abdominal pain and nausea; replace fluids; correct electrolyte, glucose, and lipid abnormalities; minimize systemic complications; and manage pancreatic necrosis and infection.

FIGURE 28-1

Algorithm of guidelines for evaluation and treatment of acute pancreatitis. ERCP, endoscopic retrograde cholangiopancreatography; ICU, intensive care unit; SIRS, systemic inflammatory response syndrome.

NONPHARMACOLOGIC THERAPY

- Endoscopic retrograde cholangiopancreatography (ERCP) may be used to remove biliary tract stones.
- Patients with alcohol-related pancreatitis should receive abstinence interventions during hospitalization.
- Nutritional support is essential because AP creates a catabolic state that leads to depletion. Patients with mild-to-moderate AP should start oral feeding as soon as tolerated—typically within 24 hours—regardless of lipase levels. In severe disease, oral or enteral nutrition is recommended within 24–72 hours. Enteral feeding via nasogastric or nasojejunal tube is preferred over parenteral nutrition (PN) when possible. PN should be reserved for cases where enteral feeding cannot be initiated, is not tolerated, or fails to meet caloric needs.
- Probiotics are not recommended for the treatment of AP.

PHARMACOLOGIC THERAPY

- Patients with AP often require intravenous (IV) antiemetics for nausea. Those admitted to the intensive care unit (ICU) should receive antisecretory therapy if they are at risk for stress-related mucosal bleeding.
- Vasodilation, vomiting, and nasogastric suction commonly cause hypovolemia and electrolyte disturbances, requiring replacement. Patients should receive moderately aggressive, goal-directed fluid resuscitation immediately after diagnosis to reduce persistent systemic inflammatory response syndrome (SIRS) and organ failure. Guidelines recommend **lactated Ringer's** at 5–10 mL/kg/hr (or 250–500 mL/hr during the first 12–24 hours. In patients without hypovolemia, initial rates should not exceed 1.5 mL/kg/hr. Patients with hypovolemia should receive a 10 mL/kg bolus. Most patients need 3–4 L of fluid in the first 24 hours. Goals include preventing rises in BUN and hematocrit during the first 24–48 hours and avoiding SIRS or renal insufficiency. Crystalloids are preferred, and lactated **Ringer's** may be superior to **normal saline**.
- IV **potassium**, **calcium**, and **magnesium** correct deficiencies, and **insulin** treats hyperglycemia.
- For mild-to-moderate pain, nonopioid analgesics such as **acetaminophen** or **nonsteroidal anti-inflammatory drugs (NSAIDs)** may be used when not contraindicated. Severe pain typically requires opioids combined with nonopioids; parenteral **morphine** is often recommended because of its longer duration. Patient-controlled analgesia is appropriate when frequent dosing is needed.
- Prophylactic antibiotics are not advised in AP without infection, including predicted severe AP or sterile necrosis.

- Treat suspected or confirmed infected AP with broad-spectrum agents covering enteric gram-negative and anaerobic organisms. **Imipenem–cilastatin** (500 mg IV every 8 hours) has been widely used but is often replaced by newer carbapenems such as **meropenem**. Penicillin-allergic patients may receive a fluoroquinolone (eg, **ciprofloxacin** or **levofloxacin**) plus **metronidazole**.
- Pancreatic exocrine insufficiency may occur in moderate or severe AP; enzyme replacement can be beneficial and is often required long-term with >50% necrosis or steatorrhea. Typical adult dosing is 50,000 units of lipase with meals and half that dose with snacks, not exceeding 10,000 units/kg/day.
- Loss of pancreatic tissue can impair islet function; patients should be monitored for postpancreatitis diabetes and treated accordingly, including insulin when necessary.

EVALUATION OF THERAPEUTIC OUTCOMES

- Assess hydration status, serum electrolytes, BUN, creatinine, hematocrit, and urine output frequently—within 6 hours of presentation and throughout the first 24–48 hours.
- In mild AP, periodically reassess pain control, fluid and electrolyte balance, and nutrition based on symptoms and fluid losses.
- Fluid therapy goals include heart rate <120 bpm, mean arterial pressure 65–85 mm Hg, urine output 0.5–1 mL/kg/hr, and hematocrit 35%–44% without transfusion.
- Transfer patients with severe AP to the ICU for close monitoring of vital signs, fluid and electrolyte status, white blood cell count, glucose, **lactate** dehydrogenase, aspartate aminotransferase, albumin, hematocrit, BUN, creatinine, and international normalized ratio. Continuous hemodynamic and arterial blood gas monitoring is essential. Lipase, amylase, and bilirubin can be checked less often. Monitor for infection, pain relief, and adequate nutrition, and assess disease severity and treatment response using evidence-based tools.

CHRONIC PANCREATITIS

CLINICAL PRESENTATION

- The main features of CP include abdominal pain, malabsorption with steatorrhea, weight loss, and diabetes. Jaundice occurs in about 10% of patients.
- Pain is typically deep, penetrating, and epigastric, often radiating to the back. It may worsen with meals or at night and can be accompanied by nausea and vomiting. Leaning forward or drawing the knees to the chest may provide relief.
- Most patients develop steatorrhea and azotorrhea. Steatorrhea is often associated with diarrhea and bloating, and patients report bulky, foul-smelling stools—sometimes with visible oil droplets—occurring three to four times daily.
- Pancreatic diabetes is a late complication, often linked to pancreatic calcification.

DIAGNOSIS

- Diagnosis relies mainly on clinical presentation and either imaging or pancreatic function tests. Noninvasive imaging includes abdominal ultrasound, CT, and MRI, while invasive imaging includes endoscopic ultrasonography and ERCP.
- Serum amylase and lipase are usually normal or slightly elevated, though they may rise during acute exacerbations.
- Total bilirubin, alkaline phosphatase, and hepatic transaminases may increase with ductal obstruction, and serum albumin and **calcium** may be low in malnutrition.
- Pancreatic function tests are used when imaging is inconclusive, as adjunctive studies, or to quantify exocrine insufficiency.

TREATMENT

- **Goals of Treatment:** The primary goals in uncomplicated CP are to relieve abdominal pain, manage malabsorption and glucose intolerance, and improve quality of life. Secondary goals include delaying complications and addressing associated conditions such as depression and malnutrition.

NONPHARMACOLOGIC THERAPY

- Lifestyle modifications should include **alcohol** abstinence and smoking cessation.
- Patients with steatorrhea should eat smaller, more frequent meals.
- Reducing dietary fat is generally not recommended but may be necessary if symptoms persist despite enzyme supplementation.
- Enteral feeding via tube is advised for malnourished patients unresponsive to oral nutrition.
- Invasive procedures and surgery are primarily reserved for uncontrolled pain or complications of CP.

PHARMACOLOGIC THERAPY

- Pain can initially be managed with **acetaminophen** (325–650 mg every 4–6 hours or 1300 mg every 8 hours) with or without NSAIDs (eg, **ibuprofen** 200–400 mg every 6–8 hours), adding adjuvant agents if pain persists or disease progresses.
- Analgesic regimens should be individualized, starting with the lowest effective dose and titrating to the maximum recommended or tolerated dose before adding or substituting agents. Schedule medications around the clock rather than as needed to improve efficacy. Giving short-acting analgesics before meals may reduce postprandial pain.
- **Pregabalin** (initially 75 mg twice daily, up to 300 mg twice daily) has the strongest evidence as an adjuvant agent.
- For difficult-to-manage pain, consider selective serotonin reuptake inhibitors (eg, **paroxetine**), serotonin/norepinephrine reuptake inhibitors (eg, **duloxetine**), or tricyclic antidepressants.
- **Tramadol** (50–100 mg every 4–6 hours, maximum 400 mg/day) can be used before escalating to stronger opioids.
- Opioids should be reserved for severe or refractory pain:
 - ✓ **Codeine:** 15–60 mg every 12 hours
 - ✓ **Hydrocodone:** 10 mg every 12 hours or 20 mg daily depending on dosage form
 - ✓ **Morphine sulfate (extended-release):** 30–60 mg every 8–12 hours
 - ✓ **Oxycodone:** 2.5–10 mg every 4–6 hours
 - ✓ **Methadone:** 2.5–5 mg every 8–12 hours
 - ✓ **Hydromorphone:** 1–2 mg every 3–4 hours
 - ✓ **Fentanyl patch:** 25–100 mcg/hr every 72 hours
- Most patients with malabsorption require pancreatic enzyme supplementation to improve nutrition and reduce steatorrhea (**Fig. 28-2**). Start with 20,000–50,000 units of lipase per meal. Give half that dose with snacks. The mealtime dose can be increased up to 90,000 units. Enteric-coated microsphere formulations are preferred (**Table 28-2**). Patients should ideally eat 3–5 meals per day, and if more than one enzyme capsule/tablet is needed per meal, doses should be spread throughout the meal.
- An antisecretory agent (histamine-2 receptor antagonist or proton pump inhibitor) may enhance enzyme therapy, particularly with non-enteric-coated forms, and should be added if enzyme therapy alone is insufficient.

- Adverse effects of pancreatic enzyme supplements are rare and usually mild, but high doses can cause nausea, vomiting, diarrhea, or gastrointestinal upset. Fibrosing colonopathy is a rare but serious complication, mostly in children with cystic fibrosis on high doses long-term.
- Assess patients with CP for fat-soluble vitamin deficiencies and supplement as needed.
- Exogenous **insulin** is the primary treatment for CP-related diabetes. **Metformin** may be used in early CP and may also reduce pancreatic cancer risk.

FIGURE 28-2

Algorithm for the treatment of malabsorption and steatorrhea in chronic pancreatitis. H₂RA, histamine-2 receptor antagonist; PPI, proton pump inhibitor.

TABLE 28-2

Commercially Available Pancreatic Enzyme (Pancrelipase) Preparations

Product	Enzyme Content per Unit Dose (USP Units)		
	Lipase	Amylase	Protease
Tablets			
Viokace 10,440 lipase units	10,440	39,150	39,150
Viokace 20,880 lipase units	20,880	78,300	78,300
Enteric-Coated Beads			
Zenpep 3000 lipase units	3000	16,000	10,000
Zenpep 5000 lipase units	5000	27,000	17,000
Zenpep 10,000 lipase units	10,000	55,000	34,000
Zenpep 15,000 lipase units	15,000	82,000	51,000
Zenpep 20,000 lipase units	20,000	109,000	68,000
Zenpep 25,000 lipase units	25,000	136,000	85,000
Zenpep 40,000 lipase units	40,000	218,000	136,000
Zenpep 60,000 lipase units	60,000	252,600	189,600
Enteric-Coated Microspheres with Bicarbonate Buffer			
Pertzye 4000 lipase units	4000	15,125	14,375
Pertzye 8000 lipase units	8000	30,250	28,750
Pertzye 16,000 lipase units	16,000	60,500	57,500

Pertzye 24,000 lipase units	24,000	90,750	86,250
Enteric-Coated Microspheres			
Creon 3000 lipase units	3000	15,000	9500
Creon 6000 lipase units	6000	30,000	19,000
Creon 12,000 lipase units	12,000	60,000	38,000
Creon 24,000 lipase units	24,000	120,000	76,000
Creon 36,000 lipase units	36,000	180,000	114,000
Enteric-Coated Minitablets/Microtablets			
Pancreaze 2600	2600	10,850	6200
Pancreaze 4200 lipase units	4200	17,500	10,000
Pancreaze 10,500 lipase units	10,500	43,750	25,000
Pancreaze 16,800 lipase units	16,800	70,000	40,000
Pancreaze 21,000 lipase units	21,000	61,000	37,000
Pancreaze 37,000 lipase units	37,000	149,900	97,300

USP, United States Pharmacopeia.

EVALUATION OF THERAPEUTIC OUTCOMES

- Assess the severity and frequency of abdominal pain periodically using a standardized scale to evaluate analgesic effectiveness. Patients on opioids should receive laxatives as needed or scheduled and be monitored for constipation, dependence, and misuse.
- For those on pancreatic enzymes for malabsorption, periodically monitor body weight and stool frequency and consistency. Assess patients with CP for fat-soluble vitamin deficiencies and provide supplementation as needed.
- Carefully monitor blood glucose in diabetic patients; those with long-standing disease should undergo regular screening for nephropathy, retinopathy, and neuropathy.

See [Chapter 60, Pancreatitis](#), authored by Scott Bolesta and Kimmy Nguyen, for a more detailed discussion of this topic.